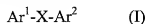


WHAT IS CLAIMED IS:

1 1. A method of treating a CCR4-mediated condition or disease in a
2 subject, said method comprising administering to a subject in need of such treatment an
3 effective amount of a compound having the formula:



5 wherein

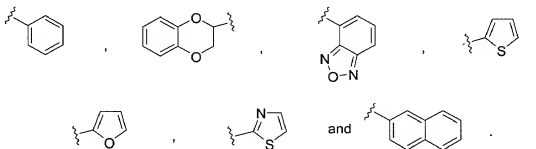
6 Ar^1 and Ar^2 are each members independently selected from the group consisting
7 of substituted or unsubstituted aryl, substituted or unsubstituted fused aryl-
8 heterocyclic ring systems and substituted or unsubstituted heteroaryl; and

9 X is a linking group selected from the group consisting of -N(R)- , -C(O)S- ,
10 $\text{-CH=CHSO}_2\text{-}$ and $\text{-SO}_2\text{N(R)-}$ wherein R is a member selected from the
11 group consisting of H and substituted or unsubstituted $(\text{C}_1\text{-C}_8)\text{alkyl}$.

1 2. A method in accordance with claim 1, wherein X is -NH- .

1 3. A method in accordance with claim 1, wherein X is $\text{-SO}_2\text{NH-}$.

1 4. A method in accordance with claim 1, wherein Ar^1 and Ar^2 are
2 each substituted or unsubstituted members independently selected from the group
3 consisting of:



1 5. A method in accordance with claim 2, wherein Ar^1 is substituted
2 heteroaryl and Ar^2 is substituted or unsubstituted aryl.

1 6. A method in accordance with claim 5, wherein said Ar^1 is a
2 substituted heteroaryl selected from the group consisting of substituted thiazolyl,
3 substituted thienyl, and substituted furanyl.

1 7. A method in accordance with claim 5, wherein said Ar² is a
2 substituted or unsubstituted phenyl or a substituted or unsubstituted naphthyl.

1 8. A method in accordance with claim 3, wherein Ar² is a phenyl
2 group having from 1 to 4 substituents independently selected from the group consisting of
3 halogen, hydroxy, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, (C₁-C₄)alkylthio, (C₁-C₄)haloalkyl, (C₁-
4 C₄)haloalkoxy, nitro, cyano, (C₁-C₄)acyl, amino, (C₁-C₄)alkylamino, and di(C₁-
5 C₄)alkylamino.

1 9. A method in accordance with claim 8, wherein said phenyl group
2 has from 1 to 3 substituents independently selected from the group consisting of halogen,
3 (C₁-C₄)haloalkyl, (C₁-C₄)haloalkoxy, nitro, cyano, and (C₁-C₄)acyl.

1 10. A method in accordance with claim 3, wherein Ar¹ is a substituted
2 or unsubstituted monocyclic or bicyclic heterocycle.

1 11. A method in accordance with claim 10, wherein said heterocycle is
2 selected from the group consisting of pyrrolyl, pyrazolyl, imidazolyl, pyrazinyl, oxazolyl,
3 isoxazolyl, thiazolyl, furyl, thienyl, pyridyl, pyrimidyl, benzothiazolyl, benzoxadiazolyl,
4 purinyl, benzimidazolyl, indolyl, isoquinolyl, quinoxalinyl and quinolyl.

1 12. A method in accordance with claim 11, wherein said heterocycle is
2 selected from the group consisting of thienyl, thiazolyl and benzoxadiazolyl.

1 13. A method in accordance with claim 1, wherein said CCR4-
2 mediated condition or disease is selected from the group consisting of contact
3 hypersensitivity, atopic dermatitis, allergic airway hypersensitivity, allergic rhinitis,
4 atherosclerosis, septic shock, angina, myocardial infarction, restenosis,
5 ischemia/reperfusion injury, multiple sclerosis, rheumatoid arthritis, type I diabetes,
6 psoriasis, cancer and HIV infection.

1 14. A method in accordance with claim 1, wherein said CCR4-
2 mediated condition or disease is psoriasis, contact hypersensitivity or atopic dermatitis.

1 15. A method in accordance with claim 14, wherein said CCR4-
2 mediated condition or disease is psoriasis.

1 **16.** A method in accordance with claim **14**, wherein said CCR4-
2 mediated condition or disease is contact hypersensitivity.

1 **17.** A method in accordance with claim **14**, wherein said CCR4-
2 mediated condition or disease is atopic dermatitis.

1 **18.** A method in accordance with claim **1**, wherein said CCR4-
2 mediated condition or disease is a disease of the airway.

1 **19.** A method in accordance with claim **18**, wherein said disease of the
2 airway is selected from the group consisting of allergic asthma and allergic rhinitis.

1 **20.** A method in accordance with claim **18**, wherein said disease of the
2 airway is allergic asthma.

1 **21.** A method in accordance with claim **1**, wherein said CCR4-
2 mediated condition or disease is a disease of innate immunity.

1 **22.** A method in accordance with claim **21**, wherein said disease of
2 innate immunity is septic shock.

1 **23.** A method in accordance with claim **1**, wherein said CCR4-
2 mediated condition or disease is atherosclerosis.

1 **24.** A method in accordance with claim **1**, wherein said CCR4-
2 mediated condition or disease is a disease or condition characterized by platelet
3 aggregation or thrombosis.

1 **25.** A method in accordance with claim **24**, wherein said CCR4-
2 mediated disease or condition is selected from the group consisting of angina, myocardial
3 infarction, restenosis, stroke and ischemia/reperfusion injury.

1 **26.** A method in accordance with claim **1**, wherein said CCR4-
2 mediated condition or disease is an allergic condition and said compound is used alone or
3 in combination with at least one therapeutic agent wherein said therapeutic agent is an
4 antihistamine.

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1 **27.** A method in accordance with claim 1, wherein said CCR4-
2 mediated disease or condition is psoriasis and said compound is used alone or in
3 combination with at least one therapeutic agent selected from a corticosteroid, a lubricant,
4 a keratolytic agent, a vitamin D₃ derivative, PUVA, or anthralin.

1 **28.** A method in accordance with claim 1, wherein said CCR4-
2 mediated disease or condition is atopic dermatitis and said compound is used alone or in
3 combination with at least one therapeutic agent selected from a lubricant and
4 corticosteroid.

1 **29.** A method in accordance with claim 1, wherein said CCR4-
2 mediated condition or disease is asthma and said compound is used alone or in
3 combination with at least one therapeutic agent selected from a β 2-agonist and a
4 corticosteroid.

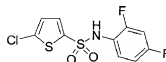
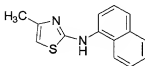
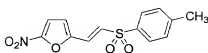
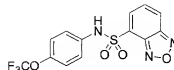
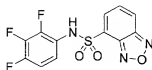
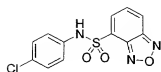
1 **30.** A method in accordance with claim 1, wherein said compound
2 interferes with the interaction between CCR4 and a ligand.

1 **31.** A method in accordance with claim 1, wherein said administration
2 is oral or intravenous.

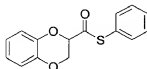
1 **32.** A method in accordance with claim 1, wherein said subject is
2 selected from the group consisting of human, rat, dog, cow, horse, and mouse.

1 **33.** A method in accordance with claim 1, wherein said subject is
2 human.

1 **34.** A method in accordance with claim 1, wherein said compound is
2 selected from the group consisting of



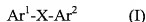
and



35. A method in accordance with claim 1, wherein said CCR4-mediated disease or condition is selected from the group consisting of multiple sclerosis, rheumatoid arthritis, type I diabetes, psoriasis, cancer and HIV infection; Ar¹ is a substituted heterocycle; X is -SO₂NH-; and Ar² is a substituted phenyl.

36. A method in accordance with claim 1, wherein said CCR4-mediated disease or condition is selected from the group consisting of multiple sclerosis, rheumatoid arthritis, type I diabetes, psoriasis, cancer and HIV infection; Ar¹ is a substituted heterocycle; X is -NH-; and Ar² is naphthyl.

37. A pharmaceutical composition for the treatment of a CCR4-mediated disease or condition, said composition comprising a pharmaceutically acceptable carrier and an effective amount of a compound which inhibits the binding of MDC or TARC to CCR4, said compound having the formula:

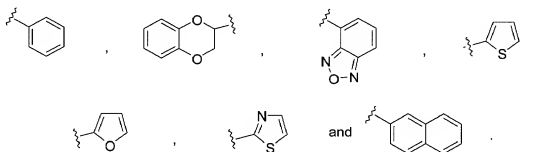


Ar¹ and Ar² are each members independently selected from the group consisting of substituted or unsubstituted aryl, substituted or unsubstituted fused aryl-heterocyclic ring systems and substituted or unsubstituted heteroaryl; and X is a linking group selected from the group consisting of -N(R)-, -C(O)S-, -CH=CHSO₂- and -SO₂N(R)- wherein R is a member selected from the group consisting of H and substituted or unsubstituted (C₁-C₈)alkyl.

38. A composition of claim 37, wherein X is -NH-.

39. A composition of claim 37, wherein X is -SO₂NH-.

40. A composition of claim 37, wherein Ar¹ and Ar² are each substituted or unsubstituted members independently selected from the group consisting of:



41. A composition of claim 37, wherein Ar¹ is substituted heteroaryl and Ar² is substituted or unsubstituted aryl.

42. A composition of claim 41, wherein said Ar¹ is a substituted heteroaryl selected from the group consisting of substituted thiazolyl, substituted thienyl, and substituted furanyl.

43. A composition of claim 41, wherein said Ar² is a substituted or unsubstituted phenyl or a substituted or unsubstituted naphthyl.

44. A composition of claim 41, wherein Ar² is a phenyl group having from 1 to 4 substituents independently selected from the group consisting of halogen, hydroxy, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, (C₁-C₄)alkylthio, (C₁-C₄)haloalkyl, (C₁-C₄)haloalkoxy, nitro, cyano, (C₁-C₄)acyl, amino, (C₁-C₄)alkylamino, and di(C₁-C₄)alkylamino.

45. A composition of claim 44, wherein said phenyl group has from 1 to 3 substituents independently selected from the group consisting of halogen, (C₁-C₄)haloalkyl, (C₁-C₄)haloalkoxy, nitro, cyano, and (C₁-C₄)acyl.

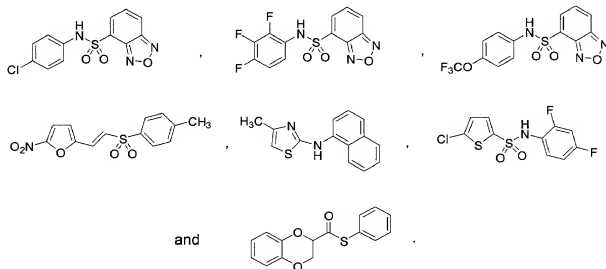
46. A composition of claim 37, wherein Ar¹ is a substituted or unsubstituted monocyclic or bicyclic heterocycle.

47. A composition of claim 46, wherein said heterocycle is selected from the group consisting of pyrrolyl, pyrazolyl, imidazolyl, pyrazinyl, oxazolyl,

isoxazolyl, thiazolyl, furyl, thienyl, pyridyl, pyrimidyl, benzothiazolyl, benzoxadiazolyl, purinyl, benzimidazolyl, indolyl, isoquinolyl, quinoxalinyl and quinolyl.

48. A composition of claim 47, wherein said heterocycle is selected from the group consisting of thienyl, thiazolyl and benzoxadiazolyl.

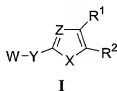
49. A composition of claim 37, wherein said compound is selected from the group consisting of



50. A method for modulating CCR4 function in a cell, comprising contacting said cell with a CCR4-modulating amount of a composition of claim 37.

51. A method for modulating CCR4 function, in which said cell is contacted with a CCR4 protein with a therapeutically effective amount of the composition of claim 37.

52. A compound of formula (I):



or a pharmaceutically acceptable salt thereof, wherein

W is selected from aryl, heteroaryl, (C₁-C₈)alkyl, heteroalkyl, cycloalkyl and heterocycloalkyl;

X is selected from N(R⁵), S, O, C(R³)=C(R⁴), N=C(R⁴) and, optionally, when Z is N, X can be C(R⁶)(R⁷);

Y is selected from a bond, N(R⁵), N(R⁵)-(C₁-C₈)alkylene, O, S and S(O)_n, wherein the integer n is 1 or 2;

Z is selected from N and C(R⁸);

R¹ and R² are independently selected from H, halogen, CN, CO₂R', CONR'R'', (C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, N(R⁶)(R⁷), OR⁹ and optionally, R¹ and R² combine to form a 5- to 8-membered ring containing from 0 to 3 heteroatoms selected from N, O and S, wherein R' and R'' are independently selected from H, (C₁-C₈)alkyl and aryl, and when R' and R'' are attached to nitrogen atom, they may be combined with the nitrogen atom to form a 5-, 6-, or 7-membered ring;

R³, R⁴ and R⁸ are independently selected from H, halogen, CN, OH, (C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, O(C₁-C₈)alkyl, N(R⁶)(R⁷) and OR⁹;

R⁵ is selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl;

R⁶ and R⁷ are independently selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl; and

R⁹ is selected from (C₁-C₈)alkyl, heteroalkyl and haloalkyl;

with the provisos that R² is other than H when W is unsubstituted phenyl, X is S, Y is NH, Z is N and R¹ is (C₁-C₈)alkyl; and R¹ is other than phenyl, when W is phenyl or unsubstituted naphthyl, X is S, Y is NH, and Z is N.

53. A compound of claim 52, wherein Z is N.

54. A compound of claim 52, wherein X is S.

55. A compound of claim 52, wherein Y is N(R⁵).

56. A compound of claim 52, wherein Z is N, X is S and Y is N(R⁵).

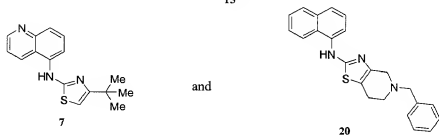
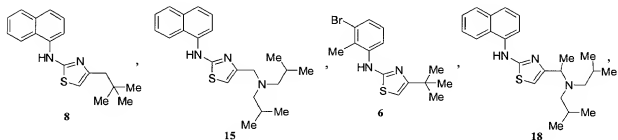
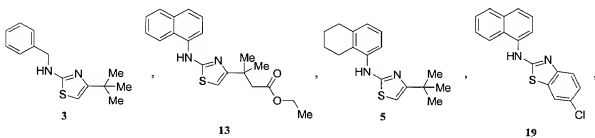
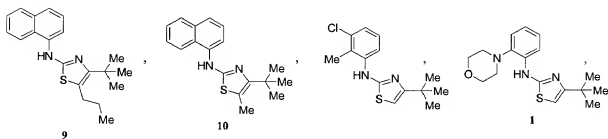
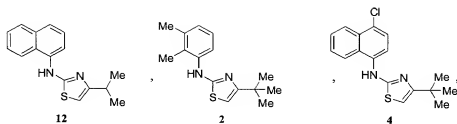
57. A compound of claim 52, wherein W is aryl or heteroaryl.

58. A compound of claim 57, wherein W is substituted or unsubstituted phenyl or naphthyl.

59. A compound of claim 57, wherein W is substituted or unsubstituted pyridyl or quinolyl.

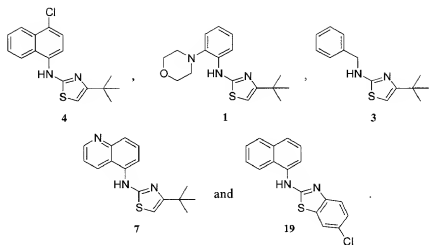
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- 1 **60.** A compound of claim **52**, wherein R¹ and R² are each
2 independently selected from H and (C₁-C₈)alkyl.
- 1 **61.** A compound of claim **52**, wherein R¹ and R² are combined to form
2 a fused 6-membered aryl or heteroaryl ring.
- 1 **62.** A compound of claim **52**, wherein Z is N, X is S, Y is N(R⁵) and
2 R¹ and R² are each independently selected from H and (C₁-C₈)alkyl.
- 1 **63.** A compound of claim **52**, wherein Z is N, X is S, Y is N(R⁵) and
2 R¹ and R² are combined to form a fused 6-membered aryl or heteroaryl ring.
- 1 **64.** A compound of claim **52**, said compound being selected from the
2 group consisting of:



and

1 65. A compound of claim 52, said compound being selected from the
2 group consisting of:



66. A compound of claim 52, wherein

W is selected from substituted phenyl, substituted or unsubstituted naphthyl, pyridyl, quinolyl, (C₁-C₈)alkyl, heteroalkyl, cycloalkyl and heterocycloalkyl;

X is selected from N(R⁵), S, O, C(R³)=C(R⁴), N=C(R⁴) and, optionally, when Z is N, X can be C(R⁶)(R⁷);

Y is selected from a bond, N(R⁵), N(R⁵)-(C₁-C₈)alkylene, O, S and S(O)_n, wherein the integer n is 1 or 2;

Z is selected from N and C(R⁸);

R¹ and R² are independently selected from H, halogen, CN, CO₂R', CONR'R'', (C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, N(R⁶)(R⁷), OR⁹ and optionally, R¹ and R² combine to form a 5- to 8-membered ring containing from 0 to 3 heteroatoms selected from N, O and S, wherein R' and R'' are independently selected from H, (C₁-C₈)alkyl and aryl, and when R' and R'' are attached to a nitrogen atom, they may be combined with the nitrogen atom to form a 5-, 6-, or 7-membered ring;

R³, R⁴ and R⁸ are independently selected from H, halogen, CN, OH, (C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, O(C₁-C₈)alkyl, N(R⁶)(R⁷) and OR⁹;

R⁵ is selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl;

R⁶ and R⁷ are independently selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl; and

R⁹ is selected from (C₁-C₈)alkyl, heteroalkyl and haloalkyl.

67. A compound of claim 66, wherein Z is N.

68. A compound of claim 66, wherein X is S.

69. A compound of claim 66, wherein Y is N(R⁵).

70. A compound of claim 66, wherein Z is N, X is S and Y is N(R⁵).

71. A compound of claim 66, wherein W is substituted phenyl or substituted or unsubstituted naphthyl.

72. A compound of claim 66, wherein W is substituted or unsubstituted pyridyl or substituted or unsubstituted quinolyl.

73. A compound of claim 66, wherein R¹ and R² are independently selected from the group consisting of H and (C₁-C₈)alkyl.

74. A compound of claim 66, wherein R¹ and R² are combined to form a fused 6-membered aryl or heteroaryl ring.

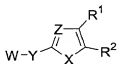
75. A compound of claim 66, wherein W is substituted phenyl or substituted or unsubstituted naphthyl, Z is N, X is S, Y is N(R⁵), and R¹ and R² are independently selected from the group consisting of H and (C₁-C₈)alkyl.

76. A compound of claim 66, wherein W is substituted phenyl or substituted or unsubstituted naphthyl, Z is N, X is S, Y is N(R⁵), and R¹ and R² are combined to form a fused 6-membered aryl or heteroaryl ring.

77. A compound of claim 66, wherein W is substituted or unsubstituted pyridyl or substituted or unsubstituted quinolyl, Z is N, X is S, Y is N(R⁵), and R¹ and R² are independently selected from the group consisting of H and (C₁-C₈)alkyl.

78. A compound of claim 66, wherein W is substituted or unsubstituted pyridyl or substituted or unsubstituted quinolyl, Z is N, X is S, Y is N(R⁵), and R¹ and R² are combined to form a fused 6-membered aryl or heteroaryl ring.

79. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of formula (I):



I

or a pharmaceutically acceptable salt thereof, wherein

W is selected from aryl, heteroaryl, (C₁-C₈)alkyl, heteroalkyl, cycloalkyl and heterocycloalkyl;

X is selected from N(R⁵), S, O, C(R³)=C(R⁴), N=C(R⁴) and, optionally, when Z is N, X can be C(R⁶)(R⁷);

Y is selected from a bond, N(R⁵), N(R⁵)-(C₁-C₈)alkylene, O, S and S(O)_n, wherein the integer n is 1 or 2;

Z is selected from N and C(R⁸);

R¹ and R² are independently selected from H, halogen, CN, CO₂R', CONR'R'', (C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, N(R⁶)(R⁷), OR⁹ and optionally, R¹ and R² combine to form a 5- to 8-membered ring containing from 0 to 3 heteroatoms selected from N, O and S, wherein R' and R'' are independently selected from H, (C₁-C₈)alkyl and aryl, and when R' and R'' are attached to nitrogen atom, they may be combined with the nitrogen atom to form a 5-, 6-, or 7-membered ring;

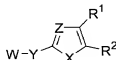
R³, R⁴ and R⁸ are independently selected from H, halogen, CN, OH, (C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, O(C₁-C₈)alkyl, N(R⁶)(R⁷) and OR⁹;

R⁵ is selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl;

R⁶ and R⁷ are independently selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl; and

R⁹ is selected from (C₁-C₈)alkyl, heteroalkyl and haloalkyl.

80. A method for treating a CCR4-mediated condition in a subject, said method comprising administering to a subject in need of such treatment an effective amount of a compound of formula (I):



I

or a pharmaceutically acceptable salt thereof, wherein

W is selected from aryl, heteroaryl, (C₁-C₈)alkyl, heteroalkyl, cycloalkyl and heterocycloalkyl;

X is selected from N(R⁵), S, O, C(R³)=C(R⁴), N=C(R⁴) and, optionally, when Z is N, X can be C(R⁶)(R⁷);

Y is selected from a bond, N(R⁵), N(R⁵)-(C₁-C₈)alkylene, O, S and S(O)_n, wherein the integer n is 1 or 2;

Z is selected from N and C(R⁸);

R¹ and R² are independently selected from H, halogen, CN, CO₂R', CONR'R'', (C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, N(R⁶)(R⁷), OR⁹ and optionally, R¹ and R² combine to form a 5- to 8-membered ring containing from 0 to 3 heteroatoms selected from N, O and S, wherein R' and R'' are independently selected from H, (C₁-C₈)alkyl and aryl, and when R' and R'' are attached to nitrogen atom, they may be combined with the nitrogen atom to form a 5-, 6-, or 7-membered ring;

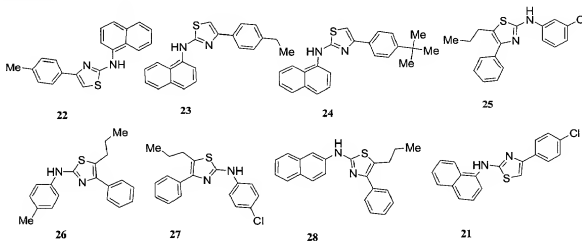
R³, R⁴ and R⁸ are independently selected from H, halogen, CN, OH, (C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, O(C₁-C₈)alkyl, N(R⁶)(R⁷) and OR⁹;

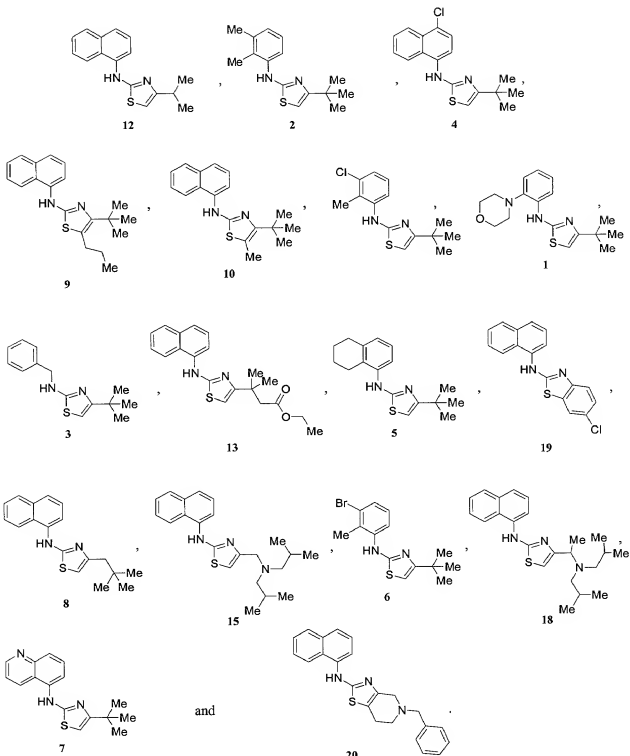
R⁵ is selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl;

R⁶ and R⁷ are independently selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl; and

R⁹ is selected from (C₁-C₈)alkyl, heteroalkyl and haloalkyl.

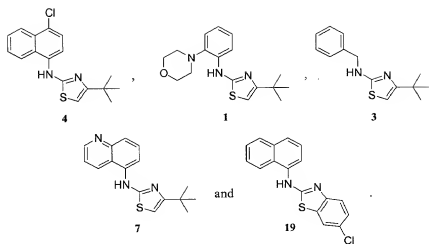
81. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound selected from the group consisting of:



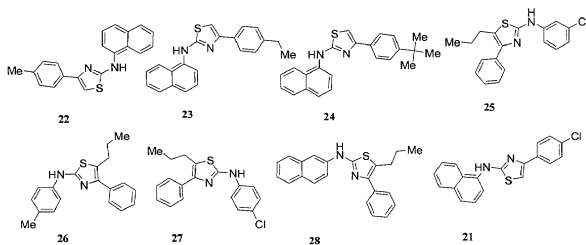


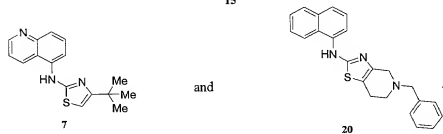
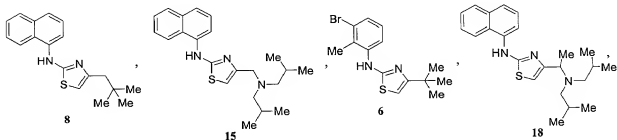
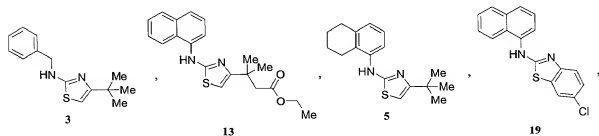
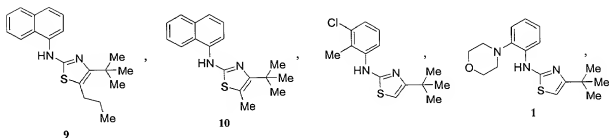
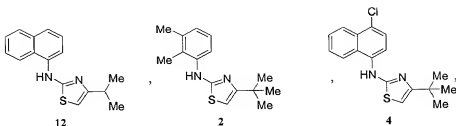
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- 1 **82.** A pharmaceutical composition of claim 81, wherein said
2 compound is selected from the group consisting of:



83. A method for treating a CCR4-mediated condition in a subject, said method comprising administering to a subject in need of such treatment an effective amount of a compound selected from the group consisting of:

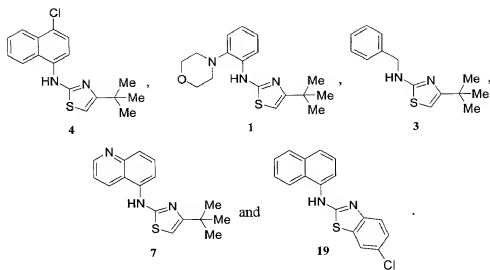




and

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1 **84.** A method in accordance with claim **83**, wherein said compound is
2 selected from the group consisting of:



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